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EXAMINER	
BRISTOL, LYNN ANNE	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketDept@uspatent.com

Office Action Summary	Application No.	Applicant(s)	
	09/852,958	SIRBASKU, DAVID A.	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-38,41-44,95-98,110-114 and 123-136* is/are pending in the application.

4a) Of the above claim(s) *44 and 96-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38,41-43,95,110-114 and 123-136* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 34-38, 41-44, 95-98, 110-114 and 123-136 are all the pending claims for this application.

2. Claims 39-40, 85, 86, 109 and 115-122 were cancelled, Claims 34, 36-38, 41-43, 95, and 110-112 were amended, and new Claims 123-136 were added in the Response of 8/12/09.

3. Claims 44 and 96-98 are withdrawn from examination.

4. Claims 34-38, 41-43, 95, 110-114 and 123-136 are the pending claims under examination.

5. Applicants amendments to the claims have necessitated new grounds for rejection. This Office Action is final.

Withdrawal of Objections

Claim Objections

6. The objection to Claims 34-43, 95 and 109-122 because of informalities is withdrawn:

a) The amendment of Claims 34-38, 41-43, 95, and 110-114 to recite "an amount of at least one immunoglobulin chosen from the group consisting of non-monomeric plasma IgA and polymeric IgM" overcomes the objection;

b) The amendment of Claims 34-38, 41-43, 95, and 110-114 to recite "nutrient medium" overcomes the objection;

c) The amendment of Claim 38 to delete the typographical error for "dimmer" overcomes the objection; and

d) The amendment of Claim 34 for the typographical error "secreted immunoglobulins" overcomes the objection.

7. The objection to Claims 35, 36, 109-112, and 115-120 for failing to further limit the subject matter of a previous claim is withdrawn with respect to the following claims:

a) As between Claims 109 and 115, both claims have been cancelled;

b) As between Claims 110 and 116, Claim 166 has been cancelled;

c) As between Claims 111 and 117, Claims 117 has been cancelled;

d) As between Claims 112 and 118, Claim 118 has been cancelled;

e) As between Claims 35 and 119, Claim 119 has been cancelled; and

f) As between Claims 36 and 120, Claim 120 has been cancelled.

Claim Rejections - 35 USC § 112, second paragraph

8. The rejection of Claims 34-43, 95 and 109-122 in lacking antecedent basis for the recitation "said steroid hormone" or because the preceding phrase "steroid hormones" encompasses a genus of steroid hormones followed by a more limiting recitation for "said steroid hormone" in Claim 34 is withdrawn.

Applicants have amended Claim 34 in the Response of 8/12/09 to recite "a steroid hormone".

9. The rejection of Claims 34-43, 95 and 109-122 for the recitation “steroid hormone-dependent cell growth stimulating effect by said substance of interest” is withdrawn.

Applicants have amended Claim 34 in the Response of 8/12/09 to delete the phrase "steroid hormone dependent effect" with respect to the effect the substance of interest has on the cell population in the assay.

10. The rejection of Claims 34-43, and 109-122 because they do not provide a relationship or correlation between the cancer cell in the preamble of Claim 34 and the predetermined population of “steroid hormone-responsive cells” in the body of Claim 34, or whether the control cells of Claim 43 are the same as the cells in Claim 34 is withdrawn.

Applicants have amended Claims 34 and 43 in the Response of 8/12/09 to clarify that the cancer cells used in the "test" sample and the "control" sample are the same.

11. The rejection of Claims 38 and 42 in lacking antecedent basis for the limitation "said immunoglobulin inhibitor" is withdrawn.

Applicants have amended Claims 34 and 43 in the Response of 8/12/09 to delete the phrase for "said immunoglobulin inhibitor".

12. The rejection of Claim 43 because it is not clear what the relationship or correlation is for the "inactivated immunoglobulin inhibitor" to the cell growth promoting effect of the substance of interest is withdrawn.

Applicants have amended Claim 43 in the Response of 8/12/09 to delete the phrase for "comprising a quantity of inactivated immunoglobulin inhibitor that is incapable of inhibiting cell growth".

13. The rejection of Claim 95 for the recitation "estrogen-dependent cell growth stimulating effect by said substance of interest, whereby an estrogenic substance is detected" is withdrawn.

Applicants have amended Claim 95 in the Response of 8/12/09 to delete the phrase "estrogen-dependent cell growth stimulating effect by said substance of interest, whereby an estrogenic substance is detected."

14. The rejection of Claims 109 and 115 for the recitation wherein said steroid hormone-free nutrient medium (Claim 109) or said nutrient medium (Claim 115) "comprises no more than about 1μM unbound Fe(III)" is moot for the cancelled claims.

15. The rejection of Claims 114 and 122 for the recitation "(per 35-mm diameter culture dish)" is withdrawn for amended Claim 114 and moot for cancelled Claim 122.

Applicants have amended Claim 114 in the Response of 8/12/09 to delete the phrase "(per 35-mm diameter culture dish)".

Rejections Maintained

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

16. The rejection of Claims 34-38, 41-43, 95, 110-114 and 123-136 under 35 USC 112, first paragraph, is maintained because the specification does not reasonably provide enablement for a method of detecting steroid hormone-like cancer growth stimulation by a substance of interest comprising maintaining a predetermined population of steroid hormone-responsive cells in a steroid hormone-free nutrient medium comprising a quantity of non-monomeric plasma IgA and or polymeric IgM for steroid hormones sufficient to inhibit cell growth in the absence of an inhibition-reversing amount of steroid hormone wherein a substance of interest is added and cell population growth is determined.

For purposes of review, the rejection was set forth in the Office Action of 3/3/05 as follows:

> "The claims are drawn to a method of detecting steroid hormone-like cancer growth stimulation by a subject of interest comprising maintaining a predetermined population of steroid hormone-responsive cells in a steroid hormone-free nutrient medium comprising a basal nutrient fluid substantially devoid of unbound Fe(III) and containing calcium ion and comprising a quantity of immunoglobulin inhibitor sufficient to inhibit cell growth in the absence of an inhibition-reversing amount of steroid hormone. This means any immunoglobulin inhibitor sufficient to inhibit cell growth in the absence of an inhibition-reversing amount of steroid hormone.
>
> The specification teaches that the instant specification satisfies the long-felt needs for a sensitive way to screen substances for estrogenic and androgenic effects (page 15, para 0030). The specification teaches that since the early 1980's researchers have unsuccessfully tried to identify serum-borne inhibitors of steroid responsive cell growth and despite its first proposal more than fifteen years ago, the purified steroid reversible serum-borne inhibitor had not been previously described (pgs 2-4). Although patents have been issued drawn to a serum mediator that is a steroid reversible inhibitor of steroid responsive cell growth, the US Patents do not address the issues of whether there are one or more or disclose the exact chemical composition of the inhibitors (p. 6, para 0010).

The specification teaches that for the first time it is disclosed that, surprisingly, certain immunoglobulins exert a steroid hormone reversible negative regulatory effect on cancer cell growth (p. 16, para 0032). These immunoglobulin inhibitors have many immediate and potential applications as reagents for cell growth assays. For example, they are useful for *in vitro* testing of substances for estrogenic effects (or other steroid hormone-like effects) on steroid hormone responsive cell growth in a suitable assay system (p. 17, para 0039) and thus are useful for assaying agents of interest, such as drugs or environmental chemicals, for their steroid hormone-like effects on cell growth stimulation (p. 18, para 0042) as an aid to avoiding undesirable proliferative side effects of such drugs or substance *in vivo* (para bridging pages 19-20). The claimed method is useful for identifying substances that have unrecognized hormone-like properties that present health hazards (p. 36, para 0229).

As drawn to the broadly claimed immunoglobulin inhibitors, the specification teaches that IgA, IgM and certain IgGs provide negative regulation of steroid hormone responsive mucosal epithelial cancer cell growth (p. 15, para 0030) and for the first time it is disclosed, surprisingly, that certain immunoblogulins exert a steroid hormone reversible negative regulatory (inhibitory) effect on steroid responsive cancer growth. In the most preferred embodiments, the inhibitors is/are dimeric IgA (non-sIgA, polymeric IgM, IgG1 kappa and IgG2 (p. 16, para 0032). The specification exemplifies the chemical and immunological properties of the partially purified CA-PS-pool II of steroid hormone reversible inhibitors of cancer cell growth wherein the long sought after serum-borne cancer cell growth inhibitors were found to include at least IgA and IgM in Example 20, p. 124-129. The specification teaches that the series of investigations presented in the example demonstrate that a very longstanding problem has been solved (p. 129, para 0480), that is inhibitors have been identified. The specification teaches that dimeric/ polymeric plasma-derived IgA, but not serum monomeric IgA or sIgA, is a steroid hormone reversible inhibitor of steroid responsive cancer cell growth (p. 129, para 0481). The specification further teaches that plasma-derived multimeric IgM is a steroid hormone reversible inhibitor of steroid responsive cancer cell growth (p. 126, para 0472). The specification concludes the discussion of Example 20 and states that "This series of investigations demonstrate at least two immunoglobuin inhibitors in serum". There may still be other useful estrogen reversible inhibitors in serum that are yet to be identified from serum or tissue sources. The methods described in this Example have direct application to the search for new compounds that mimic the effect of the immunoglobulins as" steroid reversible inhibitors. (p. 130, para 0484). The specification teaches that a poly-Ig receptor or a poly-Ig like receptor mediates the inhibition of cell growth by IgA and IgM (p. 139, para 0514) but does not teach which poly-Ig receptor or poly-Ig like receptor could be used as target for development of compounds that mimic the immune system inhibition of cancer cell growth (pgs. 141-143).

The specification teaches that bulk purified mixtures of all subclasses of horse and rat IgG are not steroid hormone reversible inhibitors of steroid responsive cancer cell growth (p. 137, para 0510), but that additional studies demonstrated that IgG1 kappa alone was a significant steroid hormone reversible inhibitor of steroid responsive cancer cell growth. Although experiments with prostate cancer cells lines showed some steroid hormone reversible inhibition of steroid responsive cancer cell with IgG2 kappa the data was not shown (p. 138, para 0511) and it does not appear that this effect was significant as the discussion of Example 23 did not even mention IgG2 kappa. This discussion however, clearly discloses that the preference for the kappa light chain implies that a different receptor mediates the effects of this immunoglobulin as compared to IgA and IgM (p. 138 para 0512) and concludes that once it is identified, the receptor that mediates the IgG1 growth inhibition effect will provide another target for development of compounds that mimic the immune system inhibition of cancer cell growth (p. 138, para 0512).

One cannot extrapolate the teaching of the specification to the enablement of the claims because the specification clearly and repeatedly teaches that the identification of the immunoglobulin inhibitors was a "surprising" that is, an unexpected event and that fifteen years of combined research by those skilled in the art had failed to identify serum-borne inhibitors of steroid responsive cell growth and despite its first proposal more than fifteen years ago, the purified steroid reversible serum-borne inhibitors had not been previously described. Further, although patents have been issued drawn to a serum mediator that is a steroid reversible inhibitor of steroid responsive cell growth, the US Patents do not address the issues of whether there are one or more or disclose the exact chemical composition of the inhibitors. However, the instant specification only sets forth three immunoglobulin inhibitors that in fact are effective as the steroid reversible immunoglobulin inhibitors of steroid-responsive cell growth. The identification of these three factors does not predictably enable the claimed invention because the specification does not teach how to make the claimed invention. Although it appears that the binding of the inhibitory immunoglobulins is through the Fc portion of the immunoglobulins, there is no teaching of which structures of the Fc portions are required for the invention to function as claimed. The specification clearly teaches that the preference for the kappa light chain of IgG implies that a different receptor mediates the effects of this immunoglobulin as compared to IgA and IgM. The specification further teaches that **a** (emphasis added) pIgR is the target for IgA and IgM but does not identify which pIgR is the target for steroid hormone reversible inhibition. However, the specification provides no information as to structures that are common to the exemplified inhibitors that would allow one of skill to predictably make the claimed inhibitors based on a structure/function correlation. Although the specification clearly teaches that once the receptors are identified, the receptors will provide another target for the development of compounds that

mimic the immune system inhibition of cancer cell growth, there is no guidance as to the receptors to which the inhibitory immunoglobulins bind so that one could make inhibitors that would predictably mimic the immune system inhibition of cancer ell growth. Finally, although the specification teaches that there may still be other useful steroid reversible inhibitors in serum that are yet to be identified from serum or tissue sources, the specification provides no guidance as to how one would predictably identify these other useful steroid reversible inhibitors.

The specification does not teach how to extrapolate the teaching of the three identified inhibitors to the broadly claimed invention because the specification does not provide information that could be used to predictably distinguish tissue inhibitory immunoglobulins from those that are not inhibitory and the screening assays exemplified in the specification for identification and testing of inhibitory immunoglobulins do not meet the standard of 35 USC 112, first paragraph because they do not teach how to make the claimed invention.

Applicant is reminded that 35 USC 112, first paragraph does not require that the specification teach how to screen for inhibitors, but rather requires that the specification teach how to make and use the claimed invention. In particular, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention. It is clear that in the absence of an effective steroid reversible inhibitor, one would not be able to successfully use the claimed broadly claimed invention.

Given that the specification specifically teaches that the combined research of those of skill was not successful in identifying the claimed immunological inhibitors despite 15 years of research, given that the specification teaches the surprising nature of the claimed inhibitors, given that the specification teaches that the receptors to which the immunological inhibitors bind are unknown, given that the specification does not teach, other than through screening assays how to identify the claimed invention, since the structures involved with the binding of the inhibitors to their cognate receptors are unknown, it is clear that the specification does provide the necessary guidance to one of skill to enable the making of the claimed invention and if the making of the broadly claimed invention is not enabled, one would not know how to use the broadly claimed invention.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predictably make the claimed invention so that it would function as claimed with a reasonable expectation of success. In the absence of guidance or exemplification so that the broadly claimed immunological inhibitors could be predictably made, the screening assays taught are drawn only to a wish or a plan for making the claimed invention. For the above reasons, it appears that undue experimentation would be required to enable one to practice the claimed invention.

The rejection was maintained in the Office Action of 6/14/06 as follows:

"Applicant argues that the arguments and evidence set forth about drawn to the indefiniteness rejection are incorporated herein. The arguments have been considered above and have not been found persuasive for the reasons set forth above.

Applicant argues that the specification provides extensive discussion, examples, figures and data to support the enablement for the method claims at issue. The argument has been considered but has not been found persuasive because, for the reasons of record, neither the specification nor the art of record enable the invention as broadly claimed.

Applicant argues that the issue at question herein is that the method claims are used to examine substances of interest, support for which has been discussed above. The argument has been considered but has not been found persuasive because, for the reasons of record, neither the specification nor the art of record support enable the invention as broadly claimed.

Applicant argues that *Rochester v. Searle* is inapposite to the present claims because the instant issue is drawn to method claims, wherein several examples of the immunoglobulin inhibitors that may be used with the method are taught and their effects clearly demonstrated. Since steroid-like effects and agents are well known, the method of the present invention clearly provides enablement for a method of screening for agents with these steroid-like effects in conjunction with the novel immunoglobulin inhibitors. The argument has been considered but has not been found persuasive since, as set forth above, the claims as drawn to the term "steroid-hormone like" are indefinite and further because, for the reasons set forth previously, the claims are not enabled for the broadly claimed invention, wherein only "novel" immunoglobulin inhibitors are taught and the specification clearly teaches that numerous immunoglobulins do not act as immunoglobulin inhibitors that inhibit cell growth in the absence of an inhibition-reversing amount of steroid hormone. Further, Applicant mischaracterizes the rejection since *Rochester v.*

Searle was not cited in regard to the claimed method, but rather in regard to the broadly claimed immunoglobulin inhibitors. Further, it is noted that this grounds of rejection does not rest on the *Rochester v. Searle* case-law.

Applicant further argues that no agents with steroid-like effects have been claimed as was the case with the claims at issue in *Rochester v. Searle*. The argument has been considered but has not been found persuasive since the issue raised is not drawn to the claimed agents, but rather is drawn to the broadly claimed immunoglobulin inhibitors.

Applicant argues that what is well-known is best omitted from the specification and that all that is necessary is that one skilled in the art be able to practice the claimed invention. Given the level of knowledge and skill in the art and in the present invention, the key enabling agent is the inhibitory immunoglobulin that enables the method that is used to examine the potential substance of interest. The arguments have been considered and have not been found persuasive. The rejection is not drawn to the identified novel immunoglobulin inhibitors, but to the scope of the claims for the reasons set forth previously and above. Further, the omitted information is not well-known or even known in the art and one skilled in the art is not able to practice the invention as broadly claimed because neither the specification nor the art of record provide sufficient guidance to enable the scope of the claims. Applicant is correct. The key enabling agent is the inhibitory immunoglobulin and for the reasons of record, none of the originally filed specification, claims or art of record enable the broadly claimed invention.

Applicant points out that Examiner makes the assumption that because data was not shown for IgG2-kappa and that its discussion was not followed up in the Example 23, that somehow its effect was not significant. Applicant disagrees with Examiner's assumption and argues that the best evidence of the meaning of the specification is the specification itself wherein Applicant points to the teachings wherein the invention is reduced to practice. The argument has been considered but has not been found persuasive because, for the reasons of record, the broadly claimed invention is not enabled. Further, as drawn to IgG2-kappa, although Applicant disagrees with Examiner's assumption and points to the specification as the best evidence of the meaning of the specification, it is clear that the specification is ambiguous at best. One might wonder why, given Examiner's clear questioning of the information in the specification, Applicant did not simply submit objective evidence demonstrating the efficacy of IgG2-kappa if such efficacy exists.

Applicant points to pages 12-13 and asks the office if it has caselaw to present that supports the statement that "one cannot extrapolate from the specification to the enablement of the claims". Further, Applicant stands ready to traverse and address any such caselaw. The request has been noted but Examiner is not clear as to why Applicant is asking for citations of case law to support a statement conventionally used in patent prosecution.

Applicant argues that Applicant has no preference for Fc receptor and all equivalent Fc receptors fall within the scope of the claims. The argument has been considered but has not been found persuasive because it is unknown what "equivalent Fc receptors" might be and Applicant is not addressing the issue raised. The issue raised is not that the exact nature and structure of any particular Fc receptor must be provided but that the surprising identification of three immunoglobulins that are useful in the claimed invention does not predictably enable the broadly claimed invention because the specification does not teach how to make the claimed invention. Examiner simply points out that the absence of guidance as to the receptors that effective immunoglobulins bind is a defect of the specification because that information might have been used as guidance for predictably identifying the broadly claimed inhibitors.

Applicant argues that methods of isolating immunoglobulin inhibitor in four species are taught and therefore Examiner's statement on page 14 that in the absence of an effective inhibitor, one would not be able to successfully use the claimed broadly claimed invention is not applicable to the present invention. The argument has been considered but has not been found persuasive because Applicant is mischaracterizing Examiner's arguments on page 14 which are drawn not only to *Rochester v. Searle* (from which section the isolated quotation is drawn) but also to the lack of teaching in the specification on how to predictably identify other and make other useful steroid reversible immunoglobulin inhibitors.

Applicant argues that, contrary to Examiner's statements, the specification provides 148 figures and 28 examples in 814 paragraphs that support the method as claimed. The argument has been considered but has not been persuasive because none of the 148 figures 28 examples or 814 paragraphs enable the broad scope of the claimed invention.

The arguments have been considered but have not been found persuasive for the reasons set forth above and the rejection is maintained.

It is further noted that Applicant did not address the issues drawn to (1) the surprising nature of the discovery upon which the invention is based, (2) the fifteen year search for serum borne inhibitors of steroid responsive cell growth, (3) the lack of guidance in the specification as how to predictably identify other useful steroid reversible inhibitors, (4) how to distinguish tissue inhibitory immunoglobulins from those that are not inhibitory."

The rejection was maintained in the Office Action of 2/12/09 as follows:

"Applicants' allegations on p. 6 of the Response of 12/14/06 have been considered and are not found persuasive. Applicants allege "The claims have been amended to specifically address the nature of the immunoglobulins as being secreted immunoglobulins that have a specific effect, that is, they inhibit steroid hormone activity. It is indeed a surprising finding that these secreted immunoglobulins were able to have the activity that had, heretofore, been unknown. As for the search for the serum inhibitors, Applicant notes that it is, in fact, secreted immunoglobulins that have traversed the secretory epithelium (along with secretory component) that have been found to have the activity, not serum borne inhibitors. The claims have been amended accordingly. Finally, ***it is not possible at this point to distinguish between those immunoglobulins that have the anti- steroidal effect***, however, the limitations include that the immunoglobutins have been secreted (thereby limiting the isotypes of immunoglobulins involved) and the heretofore unknown effect."

Response to Arguments

Applicants specification does not meet the requirement under 112, first paragraph because they have not characterized a critical element required for the ordinary artisan to reproduce or practice the method. Applicants' invention is simply a wish that some as yet uncharacterized epithelial cell-secreted antibody has the ability to inhibit steroid hormones and that an ordinary artisan could obtain from any population of heterogeneous, secretory antibodies some subset that would inhibit any steroid hormone. The specification provides no information as to structures that are common to the exemplified secretory immunoglobulin inhibitors that would allow one of skill to predictably make the claimed inhibitors based on a structure/function correlation. Although the specification clearly teaches that once the receptors are identified, the receptors will provide another target for the development of compounds that mimic the immune system inhibition of cancer cell growth, there is no guidance as to the receptors to which the inhibitory, secretory immunoglobulins bind so that one could make inhibitors that would predictably mimic the immune system inhibition of cancer ell growth. By Applicants own admission of record that they have yet to resolve the identity of any anti-steroid Ig further substantiates the outstanding rejection on the grounds that the ordinary artisan could not even practice the method much less identify a substance of interest."

Applicants allegation on pp. 10-11 of the Response of 8/12/09 have been considered and are not found persuasive. Applicants allege the amended claims, to specify non-monomeic plasma IgA and/or polymeric IgM, are enabled for providing negative regulation of steroid hormone responsive mucosal epithelial cancer cells.

Response to Arguments

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993)).

The specification demonstrates IgA and IgM provide negative regulation of steroid hormone responsive *mucosal epithelial* cancer cell growth (p. 15, para 0030). In the most preferred embodiments, the inhibitors is/are dimeric IgA (non-sIgA) and polymeric IgM (p. 16, para 0032). The specification exemplifies the chemical and immunological properties of the partially purified CA-PS-pool II of steroid hormone reversible inhibitors of cancer cell growth wherein the long sought after serum-borne cancer cell growth inhibitors were found to include at least IgA and IgM in Example 20, p. 124-129. The only mucosal epithelial cancers tested in vitro for the dimeric IgA and/or the polymeric IgM inhibiting effect on steroid-hormone growth promotion on the cancer cells: MTW9/PL2 rat mammary cells, GH4C1, GH1 and GH3 rat pituitary cells, ZR-75-1 human breast cancer cells, MCF-7A and MCF-7K human breast cancer cells, T47D human breast cancer cells, H-301 Syrian hamster kidney cells, LNCaP human prostate cancer cells, and HT-29 human colon cancer cells (Ex. 21).

The Examiner has established an evidentiary basis to support the conclusion that dimeric IgA (non-sIgA) and polymeric IgM are inhibitory for steroid hormone-induced cell proliferation of the above-mentioned cancers. Therefore, the specification provides an enabling disclosure of these reagents in the instant claimed method.

The rejection is maintained.

Written Description

17. The rejection of Claims 34-38, 41-43, 95, 110-114 and 123-136 under 35 USC 112, first paragraph, is maintained for lack of written description support for the anti-steroid, secretory immunglobulins.

For purposes of review, the rejection was set forth in the Office Action of 3/3/05 as follows:

"Claims 34- 39, 41-43, 95, 109-114 are drawn to steroid reversible inhibitors of steroid hormone-responsive cell growth. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that [a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name,of the claimed subject matter sufficient to distinguish it from other materials. Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as vertebrate insulin cDNA or mammalian insulin cDNAwithout more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of steroid reversible inhibitors of steroid hormone-responsive cell growth, per Lilly by structurally describing a representative number of steroid reversible inhibitors of steroid hormone-responsive cell growth or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, per Enzo, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In this case, the specification does not describe the steroid reversible inhibitors of steroid hormone-responsive cell growth required to practice the claimed method in a manner that satisfies either the Lilly or Enzo standards. The IgG1 kappa inhibitor disclosed does not appear to share a relevant structure with polymeric/multimeric IgA or multimeric IgM. In addition, given the surprising nature of the discovery, the combination

of the polymeric/multimeric IgA and the multimeric IgM do not provide a representative number of immunological inhibitors that would meet the requirements of Lilly. Further, the specification does not provide any functional characteristics coupled with a known or disclosed correlation between structure and function as drawn to the inhibitory activity. Although the specification discloses three effective immunological inhibitors, this does not provide a description of the steroid reversible inhibitors of steroid hormone-responsive cell growth that would satisfy the standard set out in Enzo, or describe structural features common to the members of the genus, which features constitute a substantial portion of the genuswhich would satisfy the standard set out in Lilly.

Since the specification fails to adequately describe the broadly claimed steroid reversible inhibitors of steroid hormone responsive cell growth, it also fails to adequately describe the assay method of using the claiming invention.

14. In the interests of compact prosecution, if Applicant were to amend the claims to recite further clarify the claimed inhibitors, for example to recite the limitation "comprising a steroid hormone reversible inhibitor, wherein said inhibitor consists of an immunoglobulin or a combination of immunoglobulins", and if Applicant were able to overcome the rejections under 35 USC 112, first and second paragraph above, Claims 34-43, 95, 109-113 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method of detecting steroid hormone-like cancer growth stimulation by a subject of interest comprising maintaining a predetermined population of steroid hormone-responsive cells in a defined steroid free nutrient medium comprising l.0 ng/mL to 10 ng/mL insulin, 0.3 - 10 nM triiodothyronine, 2 - 50 ug/mL- diferric transferrin, 5 - 100 gM elhanolamine, 0.2 - 5.0 mg/mL- bovine serum albumin (BSA), 5 - 20 ng/mL - selenium, 2 - 10 MM deferoxamine, and depending upon the requirements of the selected cells to be cultured, at least one compound chosen from the group consisting of 1 - 50 ng/mL EGF, 0.2 - 20 ng/mL - aFGF, 5 - 50 MM phosphoethanolamine, 50 - 500 ug/mL linoleic acid-BSA, 1 - 50 ug/mL reduced glutathione, 0.5 - 2.0 mM glutamine, 1 - 10 ug/mL heparin, and
20 - 50 ug human fibronectin (per 35-mm diameter culture dish) wherein the nutrient medium further comprises no more than about 1 uM unbound Fe(III) and contains about 1-50 mM calcium ion does not reasonably provide enablement for the claimed method of detecting steroid hormone-like cancer growth stimulation by a subject of interest comprising maintaining a predetermined population of steroid hormone-responsive cells in a steroid free nutrient medium wherein said medium comprises a basal nutrient fluid substantially devoid of unbound Fe(III) and containing calcium ion. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is noted that in view of the indefinite nature of the claim language drawn to "steroid hormone-like cancer cell growth stimulation" in claim 34, it is assumed for examination purposes that steroid hormone-like cancer cell growth stimulation , claimed in claim 34 and the claims dependent thereon as well as the estrogen-like cancer growth stimulation claimed in claim 95, is stimulation wherein the inhibitory action of immunological inhibitors of cell growth in steroid hormone-responsive cells is reversed.

The claims are drawn to a method of detecting steroid hormone-like cancer growth stimulation by a subject of interest comprising maintaining a predetermined population of steroid hormone-responsive cells in a steroid free nutrient medium wherein said medium comprises a basal nutrient fluid substantially devoid of unbound Fe(III) and containing calcium ion. This means any medium as long as it is a basal nutrient fluid substantially devoid of unbound Fe(III) and it contains calcium ion.

> The specification teaches that in order to grow the cells used in the presently described studies, the formulations of serum-free defined medium employed are specific optimizations, modifications, or necessary changes of earlier media that have been described (p. 89, para 0355). The formulations presented permit dissection of growth into its individual parts caused by different stimulators. Said serum-free medium provides a tool for the assessment of growth inhibitors isolated from horse serum whose actions are reversed by sex-steroid hormones. Thus the serum-free media raises the hope for the provision of a new insight that could help to clarify the mechanisms involved in the control of breast, prostatic and other mucosal cancers under conditions not previously available (p. 95, para 0374).

The specification teaches that it is widely believed that the phenol red indicator in tissue culture medium acts as a weak estrogen and at the concentration in standard culture media, it was believed to stimulate ER+ cell growth nearly as well a natural estrogens (para 0318). However, using the defined steroid free nutrient medium taught in the specification it was possible to determine that the concentration of phenol red contaminants in a standard culture medium today is not sufficient to cause estrogenic effects. Demonstration of sex hormone mitogenic effects in culture depends upon conditions that maximize the effects of a serum-borne inhibitor as described in the Examples. When the effects of the inhibitor are optimized, the presence or absence of phenol red makes no everyday difference to the demonstration of estrogen mitogenic effects with several target cell types from diverse species (p. 74, para 0319). The specification specifically teaches the composition of serum free defined media and serum-free media variations in TABLE 7 and on pages 93-94. Further the specification teaches that the media described in TABLE 7 were optimized for the specific cell types designated. Additionally, they were optimized to permit direct comparison of the growth properties of ER+ and AR+ steroid hormone sensitive tumor cell lines to their ER- and AR- steroid hormone

insensitive counterparts. This careful optimization was done originally to study rat mammary tumor cells. The specification discloses that previously, there was a defined medium for the prostate cancer cell line PC3, but that this medium was evaluated and did not support LNCaP prostate cancer cell line growth. Although other have reported "serum-free' media that was stated to be effective with the LNCaP cell lines, the problem was that this medium was not serum-free nor was it defined. Under those conditions, an accurate analysis of hormonal and growth factor effects cannot be done satisfactorily (p. 98). The new serum-free defined medium serves as part of a model system for identifying physiologically relevant new molecules. When completely serum-free defined conditions were employed in the past, the effects of estrogens were either marginal or insignificant (p. 104, para 0399).

One cannot extrapolate the teaching of the specification to the scope of the claims because the specification clearly teaches that the "new" serum-free defined medium is a critical element of the claimed invention. The specification clearly teaches that in order to grow the cells used in the presently described studies, the formulations of serum-free defined medium employed are specific optimizations, modifications, or necessary changes of earlier media that have been described and that the formulations presented permit dissection of growth into its individual parts caused by different stimulators and exemplifies the inability of standard culture media to permit dissection of growth into its individual parts caused by different stimulators. In particular, the specification teaches that when completely serum-free defined conditions were employed in the past, the effects of estrogens were either marginal or insignificant. Specifically, the new media were carefully optimized to permit direct comparison of growth properties of ER+ and AR+ steroid hormone sensitive tumor cell lines and their ER- and AR- steroid hormone insensitive counterparts. Further, the specification teaches that although others have reported "serum-free" media that was stated to be effective, for example, for growing the LNCaP prostate cancer cell line, the problem with this medium was that it was not in fact serum-free, nor was it defined. Under those conditions, an accurate analysis of hormonal and growth factor effects **cannot** (emphasis added)be done satisfactorily. The new serum-free defined medium serves as part of a model system for identifying physiologically relevant new molecules. Although the specification specifically states that the formulations of serum-free defined medium employed are specific optimizations, modifications, or necessary changes of earlier media that have been described and that the formulations presented permit dissection (for the first time) of growth into its individual parts caused by different stimulators, the specification provides only a single example of a medium that will function as claimed with defined variations depending upon the requirements of the selected cells to be cultured but does not teach how to successfully use the claimed invention with any other medium. This is critical because the specification specifically teaches that when completely serum-free defined conditions were employed in the past, the effects of estrogens were either marginal or insignificant and that in the absence of the defined medium, an accurate analysis of hormonal and growth factor effects **cannot** (emphasis added) be done satisfactorily. It is clear that in years of research, no other media/defined media has been found to be effective to function as claimed. The single example of a steroid hormone-free nutrient medium, modifiable for specific cell lines, does not provide guidance for how one would make any other medium that produces conditions that that maximize the effects of a serum-borne inhibitor as described in the Examples. Although experimentation to provide optimization is not considered undue, the specification does not teach the "necessary" changes of earlier media that are required so that one could make a medium that would function as claimed. Thus, the specification does not provide guidance on how one would make the claimed invention. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention in the absence of the defined medium taught in the specification.

The rejection was maintained in the Office Action of 6/14/06 as follows:

"Applicant argues that the arguments and evidence presented above are also incorporated in the instant response. The arguments and evidence have been considered above and have not been found persuasive for the reasons set forth above.

Applicant argues that Examiner's recitation of *Eli Lilly* and *Enzo* is not appropriate since they are drawn to product cases and the instantly claimed invention is a method. The argument has been considered but has not been found persuasive because Applicant appears to misunderstand the issue raised. The issue raised is that not that there is no adequate written description of the method, but rather, like the products of *Eli Lilly* and *Enzo*, there is no adequate written of products critical to the method claimed. In the absence of a written description of critical elements, the method claims lack adequate written description.

Applicant requests that Examiner cite case law to support the written description rejection. The request has been considered and Examiner suggests that Applicant review the action mailed on March 3, 2005, Section 13, pages 15-18 wherein case law that supports the written description rejection is cited.

Applicant agues that the claims presently at issue are method claims that may be used to test "substances of interest" A phrase that was established and has received the imprimatur of the office and challenges the office to withdraw any patent using the phrase from issue if case law is not produced. The argument has been considered but it appears that Applicant has not carefully read the rejection set forth in Section 13 since the rejection is drawn to the broadly claimed immunoglobulin inhibitors and not to "substances of interest".

Applicant argues that specific examples have been identified and therefore the specification provides an adequate written description. The argument has been considered but has not been found persuasive for the reasons of record.

Applicant presents arguments drawn to Examiner's discussion of a possible amendment of the claims. The arguments are moot given that the possible amendment was not made.

The arguments have been considered but have not been found persuasive and the rejection is maintained."

The rejection was maintained in the Office Action of 2/12/09 as follows:

"Applicants allegations on p. 7 of the Response of 12/14/06 have been considered and are not found persuasive. Applicants allege "The arguments and evidence presented hereinabove [*in response to the enablement rejection*] is also incorporated herein by reference, as lack of written description rejections often overlap with the common nucleus of facts addressed in response to enablement rejections. Applicant believes that the claims as amended overcome the present rejections."

Response to Arguments

For purposes of brevity, the Examiner's comments set forth under section 10 above are incorporated herein in full. Under the Revised Written Description Guideline Training Materials (66 FR 1099 (Jan. 5, 2001); 1242 O.G. 168 (Jan. 30, 2001), revised 3/29/08), the claimed invention must meet the following criteria a) Actual reduction to practice; b) Disclosure of drawings or structural chemical formulas; c) Sufficient relevant identifying characteristics; d) Method of making the claimed invention; e) Level of skill and knowledge in the art; f) Predictability in the Art. Applicants have not demonstrated with any evidence the genus of isolated, secretory immunoglobulins having steroid hormone inhibitory properties. The ordinary artisan could reasonably conclude that Applicants were not in possession of the claimed genus of isolated, secretory immunoglobulins having steroid hormone inhibitory properties at the time of application filing. The rejection is maintained."

Applicants allegation on pp. 10-11 of the Response of 8/12/09 have been considered and are not found persuasive. Applicants allege the amended claims, to specify non-monomeic plasma IgA and/or polymeric IgM, are enabled for providing negative regulation of steroid hormone responsive mucosal epithelial cancer cells.

Response to Arguments

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993)).

The specification demonstrates IgA and IgM provide negative regulation of steroid hormone responsive *mucosal epithelial* cancer cell growth (p. 15, para 0030). In the most preferred embodiments, the inhibitors is/are dimeric IgA (non-sIgA) and polymeric IgM (p. 16, para 0032). The specification exemplifies the chemical and immunological properties of the partially purified CA-PS-pool II of steroid hormone reversible inhibitors of cancer cell growth wherein the long sought after serum-borne cancer cell growth inhibitors were found to include at least IgA and IgM in Example 20, p. 124-129. The only mucosal epithelial cancers tested in vitro for the dimeric IgA and/or the polymeric IgM inhibiting effect on steroid-hormone growth promotion on the cancer cells: MTW9/PL2 rat mammary cells, GH4C1, GH1 and GH3 rat pituitary cells, ZR-75-1 human breast cancer cells, MCF-7A and MCF-7K human breast cancer cells, T47D human breast cancer cells, H-301 Syrian hamster kidney cells, LNCaP human prostate cancer cells, and HT-29 human colon cancer cells (Ex. 21).

The Examiner has established an evidentiary basis to support the conclusion that dimeric IgA (non-sIgA) and polymeric IgM are inhibitory for steroid hormone-induced cell proliferation of the above-mentioned cancers and not just any cancer as embraced by the instant claims. The rejection is maintained.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 124, 127, and 129-135 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 124 and 127 are indefinite for the recitation that "Thyroid hormones" are steroid hormones. The specification does not define a thyroid hormone as being the same as a steroid hormone. The attached dictionary definitions for a "steroid hormone" and a "thyroid hormone" do not suggest the molecules as being the same or overlapping in structure and function.

b) Claims 129 and 130 are indefinite for the recitation "a steroid hormone-dependent cancer cell growth stimulating effect by said substance of interest". The step of adding anti-steroid hormone IgA and IgM to medium is seemingly to block any endogenous or background steroid hormone activity on cell proliferation in the assay. Yet, the readout for the assay in testing any substance of interest is that the substance is required to have a "steroid hormone-dependent" effect. It is not clear how a substance can mediate a cell-proliferating effect through a steroid hormone-dependent pathway in the absence of any steroid hormone in the medium.

c) Claims 131 and 132 are indefinite for the recitation "an estrogenic dependent cancer cell growth stimulating effect by said substance of interest". The step of adding

anti-estrogenic IgA and IgM to medium is seemingly to block any endogenous or background estrogen activity on cell proliferation in the assay. Yet, the readout for the assay in testing any substance of interest is that the substance is required to have an "estrogen-dependent" effect. It is not clear how a substance can mediate a cell-proliferating effect through an estrogen-dependent pathway in the absence of any estrogen in the medium.

d) Claims 133-135 are indefinite for reciting the steps for making the steroid hormone-depleted serum when the elected invention is a screening method for a substance. The method steps for preparing serum do not in any way further define and characterize the method for screening a substance of interest.

e) Claim 135 contains the trademark/trade name "XAD™". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an Amberlite-based resin and, accordingly, the identification/description is indefinite.

f) The term "substantially" in the phrase "a substantially steroid hormone-depleted serum" of claim 135 is a relative term which renders the claim indefinite. The

term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

19. Claims 123, 125, 126, and 128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 123, 125, 126, and 128 recite "MCF-K human breast cancer cells". The examiner's search of the specification for the limitation does not identify literal support for this limitation. The search of the ATCC website for a cell line designated by this name did not reveal any matches (see attached sheet from ATCC website search). MPEP 706.03(m) states in part "New matter includes not only the addition of wholly unsupported subject matter, but may also include adding specific percentages or compounds after a broader original disclosure, or even the omission of a step from a method. See MPEP § 608.04 to § 608.04(c). See In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976) and MPEP § 2163.05 for guidance in determining whether the

addition of specific percentages or compounds after a broader original disclosure constitutes new matter."

This is a new matter rejection.

Biological Deposit

20. The claims 123, 125, 126, and 128 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (a) known and readily available to the public; (b) reproducible from the written description.

It is unclear if a cell line for MTW9/PL2, MCF-7A, or H-301 having the exact physical and chemical identity is known and publicly available, or can be reproducibly isolated without undue experimentation. The examiner's search of the ATCC website for public deposits for any of these cell lines did not identify any matches (see attached search outputs). Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the claimed cell line is an unpredictable event.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature

and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-

replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Conclusion

21. No claims allowed.

22. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LYNN BRISTOL whose telephone number is (571)272-6883. The examiner can normally be reached on 8:00-4:30, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lynn A. Bristol/
Primary Examiner, Art Unit 1643